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Lifestyle components

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Published in:
IJC Heart & Vasculature

DOI:
[10.1016/j.ijcha.2020.100492](https://doi.org/10.1016/j.ijcha.2020.100492)

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Document Version
Publisher's PDF, also known as Version of record

Publication date:
2020

[Link to publication in University of Groningen/UMCG research database](#)

Citation for published version (APA):

Siland, J. E., Zwartkruis, V., Geelhoed, B., de Boer, R. A., van Gelder, I. C., van der Harst, P., & Rienstra, M. (2020). Lifestyle components: Self-reported physical activity, nutritional status, sleep quality and incident atrial fibrillation. *IJC Heart & Vasculature*, 27, [100492]. <https://doi.org/10.1016/j.ijcha.2020.100492>

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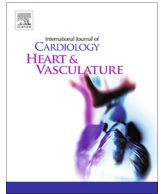
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Lifestyle components: Self-reported physical activity, nutritional status, sleep quality and incident atrial fibrillation


Recently, the role of lifestyle and incident AF has gained large interest [1]. Many of the traditional risk factors of incident atrial fibrillation (AF) as advanced age, male sex, hypertension, diabetes mellitus, myocardial infarction, heart failure, valvular heart disease, and obesity are related to lifestyle [2]. Epidemiological data of lifestyle, i.e. physical activity, nutritional status and sleep quality, and incident AF are sparse. Objectively measured lifestyle components are difficult to obtain. Instead, self-reported information obtained by standardized questionnaires could elucidate the link between lifestyle and incident AF. Besides, questionnaires could be easily incorporated in daily clinical care to assess the risk of AF. We thus investigated the association between self-reported lifestyle components via standardized questionnaires and incident AF in the large contemporary community-based cohort called Lifelines.

Lifelines (www.Lifelines.nl) is a multi-disciplinary prospective population-based cohort study and examines health and health-related behaviors in individuals of the Northern part of the Netherlands in a three-generation design [3]. Individuals were invited via their general practitioner or self-registered via the Lifelines website. Lifelines adheres to the Declaration of Helsinki, and the local ethics committee approved the study. Every participant provided written informed consent. The responding 167,729 individuals completed questionnaires on medical history, use of medication and health behaviors. They underwent medical examinations between 2006 and 2013 with the first follow-up visits between 2013 and 2017. Electrocardiograms (ECGs) were performed by trained research assistants as previously described [4]. ECG based diagnosis of AF at baseline was defined as prevalent AF, and new-onset ECG based diagnosis of AF detected at the follow-up visit was defined as incident AF. We studied three self-reported lifestyle components: physical activity, nutritional status and sleep quality. Physical activity was estimated by the Short Questionnaire to Assess Health-enhancing Physical Activity score (combination of activity, intensity and Metabolic Equivalent of Task scores in minutes per week per activity) [3] with higher scores indicating more physical activity per day. Nutritional status was inventoried by the Mini Nutritional Assessment screening score (0–14 points) [4,5] with lower scores indicating worse nutritional status. Sleep quality was assessed by the Pittsburgh Sleep Quality Investigation (0–21 points) [6] with higher scores indicating lower sleep quality. The definitions of cardiovascular risk factors and associated diseases were previously described [7].

Numbers were presented as counts (percentage) and continuous variables as mean and standard deviation (SD) or, and if not

normally distributed, as median (interquartile range). First a univariate logistic regression analyses was performed. Physical activity, nutritional status and sleep quality, were used as continuous variables and additionally divided into tertiles in the univariate logistic regression. Age- and sex adjusted variables with a $p < 0.1$ were included in a stepwise multivariable model. In the final multivariable model a p value < 0.05 was considered statistically significant. All analyses were performed using R package (Version 3.1.3; R Foundation for Statistical Computing, Vienna, Austria).

We considered 152,728 individuals, all 18 years and older. Those with prevalent AF ($n = 262$), and those with missing ECG data ($n = 53,500$) were excluded, leaving 98,966 individuals (58.5% women, mean age 45 SD 13 years) (Table 1). After a mean follow-up duration of 46 (36–55) months, incident AF was detected in 249 (0.3%) individuals.

None of the self-reported lifestyle components were associated with incident AF in univariate logistic regression (Fig. 1). In addition, results did not change when the variables of interest were divided in tertiles. Additionally, we built a stepwise multivariate model and tested all univariate significant variables. The following traditional risk factors were associated with incident AF: advanced age (odds ratio (OR) 1.13 (95% confidence interval (CI) 1.12–1.14), $p < 0.001$), sex (OR 0.35 (95% CI 0.26–0.47), $p < 0.001$), body mass index (BMI) (OR 1.10 (95% CI 1.06–1.13), $p < 0.001$), heart failure (OR 2.23 (95% CI 1.21–4.09), $p = 0.010$) and previous stroke (OR 3.02 (95% CI 1.70–5.37), $p < 0.001$). Results remained similar when individuals > 60 years of age were analyzed (data not shown).

In the Lifelines cohort with relatively young individuals, self-reported lifestyle components were not associated with incident AF.

Our results regarding physical activity are in line with a large meta-analysis with 511,503 individuals, which showed that increased physical activity is not associated with incident AF [8]. In later studies physical activity was associated with incident AF [9,10]. However, another questionnaire was used compared to our study, cardiorespiratory fitness was measured and AF ascertainment differed [3]. This may explain our different results.

In contrast to BMI, self-reported nutritional status was not associated with incident AF. However, nutritional status should not be considered a proxy of BMI, and a similar association with AF should not be expected. The questionnaire of nutritional status covers also other aspects than anthropomorphic measures, like appetite, difficulty in the digestive tract and (neuro)psychological stress.

Recently, objectively measured sleep disturbances were associated with incident AF [11]. In our study sleep disturbances are included in the sleep quality questionnaire. However, other factors included in the sleep quality questionnaire may have neutralized the risk of incident AF. Besides, self-reported questionnaires may deviate from objective measurements, as has previously been

Table 1
Characteristics of the Lifelines population.

Characteristics	Lifelines population (n = 98,966)	No AF (n = 98,717)	Incident AF (n = 249)	P-value
Age (years)	46 SD 13	46 SD 13	65 SD 10	<0.001
Sex (women)	57,952 (58.6)	57,871 (58.6)	81 (32.5)	<0.001
Cardiovascular risk factors				
Systolic blood pressure (mmHg)	124 (115–135)	124 (115–135)	133 (123–146)	<0.001
Diastolic blood pressure (mmHg)	73 (67–80)	73 (67–80)	74 (69–82)	< 0.001
Hypertension	21,146 (25.5)	21,043 (25.4)	103 (50.2)	<0.001
Diabetes mellitus	2331 (2.4)	2310 (2.3)	21 (8.5)	<0.001
Kidney disease	493 (0.5)	493 (0.5)	0 (0.0)	0.64
Body mass index (kg/m ²)	26 SD 4	26 SD 4	29 SD 5	<0.001
Associated diseases				
Previous myocardial infarction	972 (1.0)	954 (1.0)	18 (7.3)	<0.001
Previous stroke	712 (0.7)	697 (0.7)	15 (6.1)	<0.001
Heart failure	639 (0.7)	627 (0.7)	12 (5.7)	<0.001
Chronic pulmonary obstructive disease	4982 (5.1)	4965 (5.1)	17 (6.9)	0.19
Lifestyle components				
Physical activity	7200 (4680 –10,260)	7200 (4680–10,260)	6720 (4125–10,545)	0.45
Nutritional status	13 (12–13)	13 (12–13)	13 (13–13)	0.52
Sleep quality	4 (3–6)	4 (3–6)	4(3–6)	0.43

Numbers are represented as counts (percentage), continuous variables as mean SD or median (interquartile range). P-values for continuous variables are calculated with Wilcoxon test and for categorical data with Fisher exact test. Abbreviations: AF = Atrial Fibrillation, SD = standard deviation.

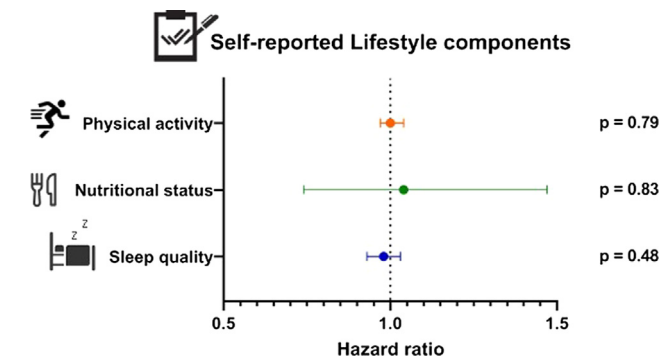


Fig. 1. Univariate logistic regression of self-reported lifestyle components and incident AF.

reported for sleep duration [12]. Inaccurate self-reported physical activity, nutritional status and sleep quality may have influenced our results.

Strengths of present analysis are the unique and large community-based cohort and use of validated questionnaires. However, AF incidence is low in this relatively young cohort and, although in accordance with other population based studies [13,14], this may have influenced our power and results. Moreover, ECGs were missing in a substantial number of Lifelines individuals and information about potential AF-related therapies was unavailable. Furthermore, the structure of Lifelines is limited in follow-up, and we therefore may have overlooked AF cases, especially paroxysmal AF episodes, and detected more persistent and permanent AF. Additionally, we have no objective measures of physical activity, nutritional status and sleep quality, and questionnaires were not collected between study visits, thus changes in lifestyle components could not be determined.

In conclusion, self-reported physical activity, nutritional status and sleep quality are not associated with incident AF, using standardized assessment tools in the community-based cohort of young individuals in Lifelines.

CRediT authorship contribution statement

Joylene E. Siland: Conceptualization, Methodology, Investigation, Writing - original draft, Project administration, Funding

acquisition. **Victor Zwartkruis:** Writing - review & editing. **Bastiaan Geelhoed:** Software, Formal analysis, Writing - review & editing. **Rudolf A. de Boer:** Writing - review & editing. **Isabelle C. van Gelder:** Writing - review & editing. **Pim van der Harst:** Writing - review & editing. **Michiel Rienstra:** Conceptualization, Supervision, Project administration.

Acknowledgements

The Lifelines Biobank is supported by the Dutch ministry of Health, Welfare and Sport, the Dutch Ministry of Economic Affairs, the University Medical Center of Groningen, University Groningen and the Northern Provinces of the Netherlands. No conflict of interest to declare.

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Received 6 December 2019

Received in revised form 21 February 2020

Accepted 22 February 2020

Available online 3 March 2020

¹ This author takes responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.